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CLAIMS

1. A method of treatment of a patient requiring analgesia which comprises the separate, simultaneous or sequential administration of a therapeutically effective amount of an opioid analgesic, devazepide and a pharmaceutically acceptable surfactant wherein the daily dosage of devazepide is up to 0.7 mg/kg/day.

2. A method of treatment of a patient undergoing opioid analgesic therapy which comprises the administration of a pharmaceutical composition comprising a therapeutically effective amount of devazepide and a pharmaceutically acceptable surfactant wherein the daily dosage of devazepide is up to 0.7 mg/kg/day.

3. A method of treatment according to claims 1 or 2 characterised in that the devazepide and surfactant are presented as a monophasic form pharmaceutical composition.

4. A method according to claims 1 or 2 characterised in that the daily dosage of devazepide is from 25 μg/kg/day to 0.7 mg/kg/day.

5. A method according to claim 4 characterised in that the daily dosage of devazepide is from 50 μg/kg/day to 0.5 mg/kg/day.

6. A monophasic pharmaceutical composition according to claim 3 characterised in that the composition is in a liquid form.

7. A method of treatment according to claim 3 characterised in that the devazepide and surfactant are in a solid dosage form.

8. A method of treatment according to claim 7 characterised in that the devazepide and surfactant are in a tablet form.

9. A method of treatment according to claim 7 characterised in that the devazepide and surfactant are in the form of a flowable powder in a capsule.

10. A method according to claims 1 or 2 characterised in that the method of delivery of the devazepide and/or the opioid is selected from the group, administration intravenously, intra-arterially, orally, intrathecally, intranasally, intrarectally, intramuscularly/subcutaneously, by inhalation and by transdermal patch.

11. A method according to claim 10 characterised in that the devazepide and/or the opioid is administered intravenously.

12. A method according to claim 11 characterised in that the intravenous administration is by intravenous bolus or a continuous intravenous infusion.

13. A method according to claim 10 characterised in that the devazepide and/or the opioid is administered subcutaneously.

14. A method according to claim 13 characterised in that the subcutaneous administration is as a subcutaneous infusion.

15. A method according to claim 10 characterised in that the devazepide and/or the opioid is administered orally.

16. A method according to claim 10 characterised in that the devazepide is administered orally.

17. A method according to claim 11 characterised in that the opioid is administered intravenously and the devazepide is administered intravenously.

18. A method according to claim 15 characterised in that the opioid is administered orally and the devazepide is administered orally.

19. A method according to claim 10 characterised in that the opioid is administered by intravenous administration or oral administration.

20. A method according to claim 10 characterised in that the opioid is administered by transdermal patch.

21. A method according to claim 16 characterised in that for oral administration the daily dosage of devazepide is from 0.07 mg/kg/day to 0.7 mg/kg/day.

22. A method according to claim 21 characterised in that for oral administration the daily dosage of devazepide is from 0.07 mg/kg/day to 0.29 mg/kg/day.

23. A method according to claim 11 characterised in that for intravenous administration the dosage of devazepide is 50 μg/kg/day to 0.5 mg/kg/day.

24. A method according to claims 1 or 2 characterised in that the opioid is selected from the group morphine, or a salt thereof such as the sulphate, chloride or hydrochloride, or the other 1,4-hydroxymorphinan opioid analgesics such as naloxone, meperidine, butorphanol or pentazocine, or morphine-6-glucuronide, codeine, dihydrocodeine, diamorphine, dextropropoxyphene, pethidine, fentanyl, alfentanil, alphaprodine, buprenorphine, dextromoramide, diphenoxylate, dipipanone, heroin (diacetylmorphine), hydrocodone (dihydrocodeinone), hydromorphone (dihydromorphinone), levorphanol, meptazinol, methadone, metopon (methyldihydromorphinone), nalbuphine, oxycodone (dihydrohydroxycodeinone), oxymorphone (dihydrohydroxymorphinone), phenadoxone, phenazocine, remifentanil, tramadol, or a salt of any of these or any combination of the aforementioned compounds.

25. A method according to claim 24 characterised in that the opioid is selected from the group hydromorphone, oxycodone, morphine, and fentanyl, and salts thereof.

26. A method according to claim 25 characterised in that the opioid is morphine or morphine sulphate.

27. A method according to claim 25 characterised in that the opioid is fentanyl, or a salt thereof.

28. A method according to claims 1 or 2 characterised in that the daily dose of surfactant is up to 0.056 mg/kg/day.

29. A method according to claims 1 or 2 characterised in that the daily dose of surfactant is from 0.4mg to 1.6mg per day.

30. A method according to claims 1 or 2 characterised in that the dosage of an opioid is from 5 to 2000mg daily.

31. A method according to claim 30 characterised in that the dosage of the opioid is from 10 to 240mg daily.

32. A method according to claim 31 characterised in that the daily dosage of the opioid is from 5 to 100mg daily.

33. A method according to claims 1 or 2 characterised in that the devazepide used in the method of the invention is substantially the S enantiomer.

34. A method according to claim 33 characterised in that the level of R enantiomer, which may be present as an impurity, is not greater than 1.5% w/w.

35. A method according to claim 1 or 2 characterised in that the surfactant is a lipophilic surfactant, a hydrophilic or a glyceride, or combinations thereof.

36. A method according to claim 35 characterised in that the surfactant is a hydrophilic surfactant.

37. A method according to claim 36 characterised in that the hydrophilic surfactant is an ionic or a non-ionic surfactant.

38. A method according to claim 37 characterised in that the hydrophilic surfactant is a non-ionic surfactant selected from the group alkylglucosides; alkylmaltosides; alkylthioglucosides; lauryl macrogolglycerides; polyoxyethylene alkyl ethers; polyoxyethylene alkylphenols; polyethylene glycol fatty acids esters; polyethylene glycol glycerol fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyglycerol fatty acid esters; polyoxyethylene glycerides; polyoxyethylene sterols, derivatives, and analogues thereof; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction mixtures of polyols and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; tocopherol polyethylene glycol succinates; sugar esters; sugar ethers; sucroglycerides; and mixtures thereof.

39. A method according to claim 37 characterised in that the hydrophilic surfactant is an ionic surfactant selected from the group alkyl ammonium salts; bile acids and salts, analogues, and derivatives thereof; fatty acid derivatives of amino acids, carnitines, oligopeptides, and polypeptides; glyceride derivatives of amino acids, oligopeptides, and polypeptides; acyl lactylates; mono-, diacetylated tartaric acid esters of mono-, diglycerides; succinoylated monoglycerides; citric acid esters of mono-, diglycerides; alginate salts; propylene glycol alginate; lecithins and hydrogenated lecithins; lysolecithin and hydrogenated lysolecithins; lysophospholipids and derivatives thereof; phospholipids and derivatives thereof; salts of alkylsulphates; salts of fatty acids; docusate sodium; and mixtures thereof.

40. A method according to claim 35 characterised in that the surfactant is a lipophilic surfactant.

41. A method according to claim 40 characterised in that the lipophilic surfactant is selected from the group alcohols; polyoxyethylene alkylethers; fatty acids; bile acids; glycerol fatty acid esters; acetylated glycerol fatty acid esters; lower alcohol fatty acids esters; polyethylene glycol fatty acid esters; polyethylene glycol glycerol fatty acid esters; polypropylene glycol fatty acid esters; polyoxyethylene glycerides; lactic acid derivatives of mono/diglycerides; propylene glycol diglycerides; sorbitan fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; transesterified vegetable oils; sterols; sterol derivatives; sugar esters; sugar ethers; sucroglycerides; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction mixtures of polyols and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; and mixtures thereof.

42. A method according to claim 41 characterised in that the surfactant is a glyceride.

43. A method according to claim 42 characterised in that the triglyceride is selected from the group vegetable oils, fish oils, animal fats, hydrogenated vegetable oils, partially hydrogenated vegetable oils, synthetic triglycerides, modified triglycerides, fractionated triglycerides, and mixtures thereof.

44. A method according to claims 1 or 2 characterised in that the surfactant is a therapeutically effective laxative and/or stool softener .

45. A method according to claims 1 or 2 characterised in that the surfactant is selected from the group alkyl sulphosuccinates, alkyl sulphates or alkyl ammonium salts.

46. A method according to claim 45 characterised in that the surfactant is selected from the group, docusate sodium (dioctyl sodium sulphosuccinate), sodium dodecyl sulphate and tetradecyltrimethyl ammonium bromide.

47. A method according to claims 1 or 2 characterised in that the surfactant also possesses antimicrobial and/or antiseptic properties.

48. A method according to claim 47 characterised in that the surfactant is cetrimide.

49. A method according to claim 46 characterised in that the surfactant is docusate sodium.

50. A method according to claims 1 or 2 characterised in that the composition comprises one or more fillers.

51. A method according to claim 50 characterised in that the filler particles are coated with surfactant, the coated filler and devazepide then being formed into an intimate mixture.

52. A method according to claim 50 characterised in that the filler is selected from the group lactose, mannitol, talc, magnesium stearate, sodium chloride, potassium chloride, citric acid, spray-dried lactose, hydrolysed starches, starch, microcrystalline cellulose, cellulosics, sorbitol, sucrose, sucrose-based materials, icodextrin, calcium sulphate, dibasic calcium phosphate and dextrose and mixtures thereof.

53. A method according to claim 52 characterised in that the filler is starch.

54. A method according to claim 53 characterised in that the starch is corn starch.

55. A method according to claim 50 characterised in that the size of the devazepide particles and the filler particles are substantially different.

56. A method according to claims 1 or 2 characterised in that the ratio of devazepide:surfactant is from 5:1 to 25:1 w/w.

57. A method according to claim 49 characterised in that the composition comprises devazepide and a surfactant with the remainder of the composition being made up with a filler.

58. A method according to claim 56 characterised in that the composition comprises 1.25mg devazepide, 0.1 mg surfactant and 148.65 mg of a filler.

59. A method according to claim 57 characterised in that the composition comprises 1.25mg devazepide, 0.1 mg docusate sodium and 148.65 mg of corn starch.

60. A method according to claim 56 characterised in that the composition comprises is 2.5mg devazepide, 0.2 mg surfactant and 297.3mg of a filler.

61. A method according to claim 59 characterised in that the composition comprises 2.5mg devazepide, 0.2mg docusate sodium and 297.3mg corn starch.

62. A method according to claims 1, 2 or 49 characterised in that the composition is filled into a capsule.

63. A method according to claim 61 characterised in that the capsule is a gelatin capsule.

64. The use of devazepide in the manufacture of a monophasic pharmaceutical composition comprising a therapeutically effective amount of devazepide and a pharmaceutically acceptable surfactant wherein the daily dosage of devazepide is up to 0.7 mg/kg/day.

65. The use according to claim 64 characterised in that the pharmaceutical composition is in solid dosage form.

66. A monophasic pharmaceutical composition comprising a therapeutically effective amount of devazepide and a pharmaceutically acceptable surfactant wherein the daily dosage of devazepide is up to 0.7 mg/kg/day.

67. A monophasic pharmaceutical composition according to claim 66 characterised in that the daily dosage of devazepide is from 25 μg/kg/day to 0.7 mg/kg/day.

68. A monophasic pharmaceutical composition according to claim 67 characterised in that the daily dosage of devazepide is from 50 μg/kg/day to 0.5 mg/kg/day.

69. A monophasic pharmaceutical composition according to claim 66 characterised in that the composition is in a liquid form.

70. A monophasic pharmaceutical composition according to claim 66 characterised in that the composition is in a solid dosage form.

71. A monophasic pharmaceutical composition according to claim 70 characterised in that the composition is in the form of a tablet.

72. A monophasic pharmaceutical composition according to claim 70 characterised in that the composition is in the form of a flowable powder in a capsule.

73. A monophasic pharmaceutical composition according to claim 66 characterised in that the composition is adapted for the separate, simultaneous or sequential administration with a therapeutically effective amount of an opioid analgesic.

74. A monophasic pharmaceutical composition according to claim 66 characterised in that the composition is adapted to be administered intravenously, intra-arterially, orally, intrathecally, intranasally, intrarectally, intramuscularly/subcutaneously, by inhalation or by transdermal patch.

75. A monophasic pharmaceutical composition according to claim 74 characterised in that the devazepide and/or the opioid is adapted to be administered intravenously.

76. A monophasic pharmaceutical composition according to claim 75 characterised in that the intravenous administration is by intravenous bolus or a continuous intravenous infusion.

77. A monophasic pharmaceutical composition according to claim 74 characterised in that the devazepide and/or the opioid is adapted to be administered subcutaneously.

78. A monophasic pharmaceutical composition according to claim 77 characterised in that the subcutaneous administration is as a subcutaneous infusion.

79. A monophasic pharmaceutical composition according to claim 74 characterised in that the devazepide and/or the opioid is adapted to be administered orally.

80. A monophasic pharmaceutical composition according to claim 74 characterised in that the devazepide is administered orally.

81. A monophasic pharmaceutical composition according to claim 75 characterised in that the opioid is administered intravenously and the devazepide is administered intravenously.

82. A monophasic pharmaceutical composition according to claim 79 characterised in that the opioid is administered orally and the devazepide is administered orally.

83. A monophasic pharmaceutical composition according to claim 74 characterised in that the opioid is administered by intravenous administration or oral administration.

84. A monophasic pharmaceutical composition according to claim 74 characterised in that the opioid is administered by transdermal patch.

85. A monophasic pharmaceutical composition according to claim 74 characterised in that for oral administration the daily dosage of devazepide is from 0.07 mg/kg/day to 0.7 mg/kg/day.

86. A monophasic pharmaceutical composition according to claim 85 characterised in that for oral administration the daily dosage of devazepide is from 0.07 mg/kg/day to 0.29 mg/kg/day.

87. A monophasic pharmaceutical composition according to claim 86 characterised in that for intravenous administration the dosage of devazepide is 50 µg/kg/day to 0.5 mg/kg/day.

88. A monophasic pharmaceutical composition according to claim 66 characterised in that the opioid is selected from the group morphine, or a salt thereof such as the sulphate, chloride or hydrochloride, or the other 1,4-hydroxymorphinan opioid analgesics such as naloxone, meperidine, butorphanol or pentazocine, or morphine-6-glucuronide, codeine, dihydrocodeine, diamorphine, dextropropoxyphene, pethidine, fentanyl, alfentanil, alphaprodine, buprenorphine, dextromoramide, diphenoxylate, dipipanone, heroin (diacetylmorphine), hydrocodone (dihydrocodeinone), hydromorphone (dihydromorphinone), levorphanol, meptazinol, methadone, metopon (methyldihydromorphinone),

nalbuphine, oxycodone (dihydrohydroxycodeinone), oxymorphone (dihydrohydroxymorphinone), phenadoxone, phenazocine, remifentanil, tramadol, or a salt of any of these, or any combination of the aforementioned compounds.

89. A monophasic pharmaceutical composition according to claim 88 characterised in that the opioid is selected from the group hydromorphone, oxycodone, morphine and fentanyl, or a salt thereof.

90. A monophasic pharmaceutical composition according to claim 89 characterised in that the opioid is morphine or morphine sulphate.

91. A monophasic pharmaceutical composition according to claim 89 characterised in that the opioid is fentanyl, or a salt thereof.

92. A monophasic pharmaceutical composition according to claim 66 characterised in that the daily dose of surfactant is up to 0.056 mg/kg/day.

93. A monophasic pharmaceutical composition according to claim 66 characterised in that the daily dose of surfactant is from 0.4mg to 1.6mg per day.

94. A monophasic pharmaceutical composition according to claim 66 characterised in that the dosage of an opioid is from 5 to 2000mg daily.

95. A monophasic pharmaceutical composition according to claim 94 characterised in that the dosage of the opioid is from 10 to 240mg daily.

96. A monophasic pharmaceutical composition according to claim 95 characterised in that the daily dosage of the opioid is from 5 to 100mg daily.

97. A monophasic pharmaceutical composition according to claim 66 characterised in that the devazepide is substantially the S enantiomer.

98. A monophasic pharmaceutical composition according to claim 97 characterised in that the level of R enantiomer, which may be present as an impurity, is not greater than 1.5% w/w.

99. A monophasic pharmaceutical composition according to claim 66 characterised in that the surfactant is a lipophilic surfactant, a hydrophilic or a glyceride, or combinations thereof.

100. A monophasic pharmaceutical composition according to claim 99 characterised in that the surfactant is a hydrophilic surfactant.

101. A monophasic pharmaceutical composition according to claim 100 characterised in that the hydrophilic surfactant is an ionic or a non-ionic surfactant.

102. A monophasic pharmaceutical composition according to claim 101 characterised in that the hydrophilic surfactant is a non-ionic surfactant selected from the group alkylglucosides; alkylmaltosides; alkylthioglucosides; lauryl macrogolglycerides; polyoxyethylene alkyl ethers; polyoxyethylene alkylphenols; polyethylene glycol fatty acids esters; polyethylene glycol glycerol fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyglycerol fatty acid esters; polyoxyethylene glycerides; polyoxyethylene sterols, derivatives, and analogues thereof; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction mixtures of polyols and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; tocopherol polyethylene glycol succinates; sugar esters; sugar ethers; sucroglycerides; and mixtures thereof.

103. A monophasic pharmaceutical composition according to claim 101 characterised in that the hydrophilic surfactant is an ionic surfactant selected from the group alkyl ammonium salts; bile acids and salts, analogues, and derivatives thereof; fatty acid derivatives of amino acids, carnitines, oligopeptides, and polypeptides; glyceride derivatives of amino acids, oligopeptides, and polypeptides;

acyl lactylates; mono-, diacetylated tartaric acid esters of mono-, diglycerides; succinoylated monoglycerides; citric acid esters of mono-, diglycerides; alginate salts; propylene glycol alginate; lecithins and hydrogenated lecithins; lysolecithin and hydrogenated lysolecithins; lysophospholipids and derivatives thereof; phospholipids and derivatives thereof; salts of alkylsulphates; salts of fatty acids; docusate sodium; and mixtures thereof.

104. A monophasic pharmaceutical composition according to claim 99 characterised in that the surfactant is a lipophilic surfactant.

105. A monophasic pharmaceutical composition according to claim 104 characterised in that the lipophilic surfactant is selected from the group alcohols; polyoxyethylene alkylethers; fatty acids; bile acids; glycerol fatty acid esters; acetylated glycerol fatty acid esters; lower alcohol fatty acids esters; polyethylene glycol fatty acid esters; polyethylene glycol glycerol fatty acid esters; polypropylene glycol fatty acid esters; polyoxyethylene glycerides; lactic acid derivatives of mono/diglycerides; propylene glycol diglycerides; sorbitan fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; transesterified vegetable oils; sterols; sterol derivatives; sugar esters; sugar ethers; sucroglycerides; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction mixtures of polyols and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; and mixtures thereof.

106. A monophasic pharmaceutical composition according to claim 99 characterised in that the surfactant is a glyceride.

107. A monophasic pharmaceutical composition according to claim 106 characterised in that the triglyceride is selected from the group vegetable oils, fish oils, animal fats, hydrogenated vegetable oils, partially hydrogenated vegetable oils, synthetic triglycerides, modified triglycerides, fractionated triglycerides, and mixtures thereof.

108. A monophasic pharmaceutical composition according to claim 66 characterised in that the surfactant is a therapeutically effective surfactant.

109. A monophasic pharmaceutical composition according to claim 66 characterised in that the surfactant is selected from the group alkyl sulphosuccinates, alkyl sulphates or alkyl ammonium salts.

110. A monophasic pharmaceutical composition according to claim 109 characterised in that the surfactant is selected from the group, docusate sodium (dioctyl sodium sulphosuccinate), sodium dodecyl sulphate and tetradecyltrimethyl ammonium bromide.

111. A monophasic pharmaceutical composition according to claim 66 characterised in that the surfactant also possesses antimicrobial and/or antiseptic properties.

112. A monophasic pharmaceutical composition according to claim 111 characterised in that the surfactant is cetrimide.

113. A monophasic pharmaceutical composition according to claim 110 characterised in that the surfactant is docusate sodium.

114. A monophasic pharmaceutical composition according to claim 66 characterised in that the composition comprises one or more fillers.

115. A monophasic pharmaceutical composition according to claim 114 characterised in that the filler particles are coated with the surfactant, the coated filler and devazepide then being formed into an intimate mixture.

116. A monophasic pharmaceutical composition according to claim 114 characterised in that the filler is selected from the group lactose, mannitol, talc,

magnesium stearate, sodium chloride, potassium chloride, citric acid, spray-dried lactose, hydrolysed starches, starch, microcrystalline cellulose, cellulosics, sorbitol, sucrose, sucrose-based materials, icodextrin, calcium sulphate, dibasic calcium phosphate and dextrose and mixtures thereof.

117. A monophasic pharmaceutical composition according to claim 116 characterised in that the filler is starch.

118. A monophasic pharmaceutical composition according to claim 117 characterised in that the starch is corn starch.

119. A monophasic pharmaceutical composition according to claim 114 characterised in that the size of the devazepide particles and the filler particles are different.

120. A monophasic pharmaceutical composition according to claim 66 characterised in that the ratio of devazepide:surfactant is from 5:1 to 25:1 w/w.

121. A monophasic pharmaceutical composition according to claim 114 characterised in that the composition comprises devazepide and a surfactant with the remainder of the composition being made up with a filler.

122. A monophasic pharmaceutical composition according to claim 121 characterised in that the composition comprises 1.25mg devazepide, 0.1 mg surfactant and 148.65 mg of a filler.

123. A monophasic pharmaceutical composition according to claim 122 characterised in that the composition comprises 1.25mg devazepide, 0.1 mg docusate sodium and 148.65 mg of corn starch.

124. A monophasic pharmaceutical composition according to claim 121 characterised in that the composition comprises is 2.5mg devazepide, 0.2 mg surfactant and 297.3mg of a filler.

125. A monophasic pharmaceutical composition according to claim 124 characterised in that the composition comprises 2.5mg devazepide, 0.2mg docusate sodium and 297.3mg corn starch.

126. A monophasic pharmaceutical composition according to claim 66 characterised in that the composition is filled into a capsule.

127. A monophasic pharmaceutical composition according to claim 126 characterised in that the capsule is a gelatin capsule.

128. A method or a composition substantially as described with reference to the accompanying examples.